

5 We Claim:

1. A process for the production of polymeric microparticles comprising dissolving a polymer in a halogen-free solvent that is at least partially water-miscible to form a polymer solution; adding a hydrophilic active agent to the polymer solution to form a drug phase contained in a vessel; adding a predetermined amount of an aqueous surfactant phase to the vessel containing the drug phase with mixing, wherein $\delta_{\text{polymer solvent}} - \delta_{\text{aqueous phase}} < 0$, said predetermined amount being sufficient to provide that the surfactant phase becomes the continuous phase and extraction medium in order to extract an amount of said solvent from said drug phase such that a suspension of microparticles is produced upon addition of the surfactant phase to the drug phase without requiring removal of solvent from the vessel.
- 10 2. A process according to claim 1 further comprising removing the solvent.
- 15 3. A process according to claim 2 wherein the solvent is removed by washing, filtration, vacuum, or evaporation.
4. A process according to claim 1 wherein the solvent has a water solubility of at least 1.5 – 40 wt% in water.
5. A process according to claim 4 wherein the solvent solubility is at least 5 wt% in water.
- 20 6. A process according to claim 5 wherein the solvent solubility is at least 10 wt% in water.
7. A process according to claim 1 wherein the volume fraction of the surfactant phase is at least 0.60.
- 25 8. A process according to claim 1 wherein the volume fraction of the surfactant phase is 0.65 – 0.75.
9. A process according to claim 1 wherein the volume ratio of polymer phase : surfactant phase is within the range 1:2 - 1:30.
10. A process according to claim 9 wherein the ratio is 1:2 – 1:20.
11. A process according to claim 1 further comprising adding a water-miscible co-solvent to the surfactant phase wherein said polymer solvent is soluble in said co-solvent and said polymer is not soluble in said co-solvent.

12. A process according to claim 11 wherein said co-solvent is selected from the group consisting of alcohols, polyethylene glycol, and ethers.

13. A process according to claim 12 wherein the co-solvent is selected from the group consisting of ethanol, methanol, isopropyl alcohol, and polyethylene glycol.

5 14. A process according to claim 1 further comprising adding a buffer to the drug solution.

15. A process according to claim 1 further comprising adding a buffer to the surfactant phase.

10 16. A process according to claim 15 wherein the polymer is not soluble in the surfactant phase.

17. A process according to claim 1 wherein the microparticles comprise microcapsules.

15 18. A process according to claim 1 wherein the microparticles comprise microsponges.

19. A process according to claim 1 wherein the microparticles comprise microspheres.

20 20. A process according to claim 1 further comprising adding a viscosity modifier to the aqueous surfactant phase.

21. A process according to claim 20 comprising 5 - 50 wt% of the viscosity modifier.

20 22. A process according to claim 21 wherein the viscosity modifier is selected from the group consisting of glycerol, hyaluronic acid, cellulose polymers and derivatives thereof, chitosane, or polyethylene glycol.

25 23. The process according to claim 14, wherein the buffered solution is selected from the group consisting of a phosphate buffer solution, a citrate buffer solution and a tris(hydroxymethyl)aminomethane solution.

24. A process according to claim 1 wherein the polymer is selected from the group consisting of polyamides, polyanhydrides, polyesters, polyorthoesters, polyacetates, polylactones, and polyorthocarbonates.

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25. A process according to claim 24 wherein the polymer is selected from the group consisting of polyesters of α -, β - and γ -hydroxycarboxylic acids, or block copolymers of polyesters of α -, β - and γ -hydroxycarboxylic acids and linear or star poly(ethylene glycols).

5 26. A process according to claim 25 wherein the polymer comprises a poly lactide co-glycolide polymer.

27. A process according to claim 1 wherein the partially water-miscible solvent is selected from the group consisting of acetone, ethanol, alkyl acetates, alkyl formates, triacetin, triethyl citrate, and alkyl lactates or mixtures thereof.

10 28. A process according to claim 27 wherein the solvent is selected from the group consisting of ethanol, acetone, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, methyl formate, ethyl formate, propyl formate, isopropyl formate, butyl formate, triacetin, methyl lactate, ethyl lactate or mixtures thereof.

15 29. A process according to claim 1 wherein the surfactant is a non-ionic surfactant.

30. Microparticles produced by the process according to any one of claims 1, 5, 8, 24, or 26.